

CLAIMS

1. An anhydrous form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Anhydrous Form B)  
5 having an X-ray powder diffraction pattern containing specific peaks at: 3.8 ( $\pm 0.1^\circ$ ), 7.5 ( $\pm 0.1^\circ$ ), 11.2 ( $\pm 0.1^\circ$ ), 13.0 ( $\pm 0.1^\circ$ ), 13.8 ( $\pm 0.1^\circ$ ), 15.0 ( $\pm 0.1^\circ$ ), 15.7 ( $\pm 0.1^\circ$ ), 18.8 ( $\pm 0.1^\circ$ ), 20.2 ( $\pm 0.1^\circ$ ), 21.7 ( $\pm 0.1^\circ$ ), 22.6 ( $\pm 0.1^\circ$ ) and 30.2 ( $\pm 0.1^\circ$ )  $2\theta$ .
2. An anhydrous form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Anhydrous Form C)  
10 having an X-ray powder diffraction pattern containing specific peaks at: 4.3 ( $\pm 0.1^\circ$ ), 8.5 ( $\pm 0.1^\circ$ ), 14.6 ( $\pm 0.1^\circ$ ), 15.3 ( $\pm 0.1^\circ$ ), 16.1 ( $\pm 0.1^\circ$ ), 17.4 ( $\pm 0.1^\circ$ ), 18.7 ( $\pm 0.1^\circ$ ), 20.5 ( $\pm 0.1^\circ$ ), 22.1 ( $\pm 0.1^\circ$ ), 22.6 ( $\pm 0.1^\circ$ ), 23.1 ( $\pm 0.1^\circ$ ) and 29.6 ( $\pm 0.1^\circ$ )  $2\theta$ .
- 15 3. A hydrated form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form A) having an X-ray powder diffraction pattern containing specific peaks at: 4.2 ( $\pm 0.1^\circ$ ), 8.2 ( $\pm 0.1^\circ$ ), 8.5 ( $\pm 0.1^\circ$ ), 9.1 ( $\pm 0.1^\circ$ ), 11.5 ( $\pm 0.1^\circ$ ), 12.7 ( $\pm 0.1^\circ$ ), 14.8 ( $\pm 0.1^\circ$ ), 15.4 ( $\pm 0.1^\circ$ ), 16.6 ( $\pm 0.1^\circ$ ), 17.4 ( $\pm 0.1^\circ$ ), 17.7 ( $\pm 0.1^\circ$ ), 18.2 ( $\pm 0.1^\circ$ ), 20.4 ( $\pm 0.1^\circ$ ), 23.2 ( $\pm 0.1^\circ$ ), 29.1 ( $\pm 0.1^\circ$ ) and 29.8 ( $\pm 0.1^\circ$ )  $2\theta$ .  
20
4. A compound as claimed in claim 3 wherein the water of crystallisation is 3-10% w/w.
- 25 5. A hydrated form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form B) having an X-ray powder diffraction pattern containing specific peaks at: 4.5 ( $\pm 0.1^\circ$ ), 7.3 ( $\pm 0.1^\circ$ ), 8.3 ( $\pm 0.1^\circ$ ), 13.3 ( $\pm 0.1^\circ$ ), 14.5 ( $\pm 0.1^\circ$ ), 14.8 ( $\pm 0.1^\circ$ ), 15.4 ( $\pm 0.1^\circ$ ), 16.6 ( $\pm 0.1^\circ$ ), 18.7 ( $\pm 0.1^\circ$ ), 20.2 ( $\pm 0.1^\circ$ ), 21.1 ( $\pm 0.1^\circ$ ), 21.5 ( $\pm 0.1^\circ$ ), 21.9 ( $\pm 0.1^\circ$ ), 22.3 ( $\pm 0.1^\circ$ ), 23.5 ( $\pm 0.1^\circ$ ) and 24.9 ( $\pm 0.1^\circ$ )  $2\theta$ .  
30
6. A compound as claimed in claim 5 wherein the water of crystallisation is 5-7% w/w.

7. A hydrated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form C) having an X-ray powder diffraction pattern containing specific peaks at: 4.2 ( $\pm 0.1^\circ$ ), 7.5 ( $\pm 0.1^\circ$ ), 8.0 ( $\pm 0.1^\circ$ ), 11.4 ( $\pm 0.1^\circ$ ), 12.5 ( $\pm 0.1^\circ$ ), 15.1 ( $\pm 0.1^\circ$ ), 15.8 ( $\pm 0.1^\circ$ ), 17.7 ( $\pm 0.1^\circ$ ), 18.9 ( $\pm 0.1^\circ$ ), 20.5 ( $\pm 0.1^\circ$ ), 21.1 ( $\pm 0.1^\circ$ ), 22.7 ( $\pm 0.1^\circ$ ), 24.6 ( $\pm 0.1^\circ$ ), 26.1 ( $\pm 0.1^\circ$ ), 27.8 ( $\pm 0.1^\circ$ ) and 29.2 ( $\pm 0.1^\circ$ )  $2\theta$ .
8. A compound as claimed in claim 7 wherein the water of crystallisation is 3-10% w/w.
9. A hydrated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form D) having an X-ray powder diffraction pattern containing specific peaks at: 8.8 ( $\pm 0.1^\circ$ ), 10.5 ( $\pm 0.1^\circ$ ), 11.8 ( $\pm 0.1^\circ$ ), 12.9 ( $\pm 0.1^\circ$ ), 15.6 ( $\pm 0.1^\circ$ ), 17.1 ( $\pm 0.1^\circ$ ), 18.9 ( $\pm 0.1^\circ$ ), 20.8 ( $\pm 0.1^\circ$ ), 23.3 ( $\pm 0.1^\circ$ ), 25.6 ( $\pm 0.1^\circ$ ), 26.1 ( $\pm 0.1^\circ$ ), 26.9 ( $\pm 0.1^\circ$ ), 28.1 ( $\pm 0.1^\circ$ ), 30.6 ( $\pm 0.1^\circ$ ), 32.5 ( $\pm 0.1^\circ$ ) and 33.1 ( $\pm 0.1^\circ$ )  $2\theta$ .
10. A solvated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Solvated Form E) having an X-ray powder diffraction pattern containing specific peaks at: 3.6 ( $\pm 0.1^\circ$ ), 7.1 ( $\pm 0.1^\circ$ ), 8.3 ( $\pm 0.1^\circ$ ), 9.3 ( $\pm 0.1^\circ$ ), 9.8 ( $\pm 0.1^\circ$ ), 14.1 ( $\pm 0.1^\circ$ ), 15.9 ( $\pm 0.1^\circ$ ), 17.7 ( $\pm 0.1^\circ$ ), 18.6 ( $\pm 0.1^\circ$ ), 19.3 ( $\pm 0.1^\circ$ ), 21.7 ( $\pm 0.1^\circ$ ), 23.1 ( $\pm 0.1^\circ$ ), 24.1 ( $\pm 0.1^\circ$ ), 25.0 ( $\pm 0.1^\circ$ ), 25.8 ( $\pm 0.1^\circ$ ) and 26.3 ( $\pm 0.1^\circ$ )  $2\theta$ .
11. A crystalline form of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) having an X-ray powder diffraction pattern containing specific peaks at: 7.3 ( $\pm 0.1^\circ$ ), 8.5 ( $\pm 0.1^\circ$ ), 10.6 ( $\pm 0.1^\circ$ ), 13.4 ( $\pm 0.1^\circ$ ), 14.7 ( $\pm 0.1^\circ$ ), 15.4 ( $\pm 0.1^\circ$ ), 15.9 ( $\pm 0.1^\circ$ ), 19.9 ( $\pm 0.1^\circ$ ), 20.2 ( $\pm 0.1^\circ$ ), 21.7 ( $\pm 0.1^\circ$ ), 25.8 ( $\pm 0.1^\circ$ ) and 26.6 ( $\pm 0.1^\circ$ )  $2\theta$ .
12. A crystalline form of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form B) having an X-ray powder diffraction pattern

containing specific peaks at: 9.9 ( $\pm 0.1^\circ$ ), 10.5 ( $\pm 0.1^\circ$ ), 11.0 ( $\pm 0.1^\circ$ ), 11.6 ( $\pm 0.1^\circ$ ), 13.3 ( $\pm 0.1^\circ$ ), 13.9 ( $\pm 0.1^\circ$ ), 14.9 ( $\pm 0.1^\circ$ ), 18.0 ( $\pm 0.1^\circ$ ), 19.0 ( $\pm 0.1^\circ$ ), 20.4 ( $\pm 0.1^\circ$ ), 22.2 ( $\pm 0.1^\circ$ ) and 23.0 ( $\pm 0.1^\circ$ ) 2 $\theta$ .

- 5 13. A pharmaceutical composition comprising a compound as claimed in claims 1 to 12 and a pharmaceutically acceptable adjuvant, diluent or carrier.
14. A compound as claimed in claims 1 to 12 for use in therapy.
- 10 15. The use of a compound as claimed in claims 1 to 12 in the manufacture of a medicament for use in therapy.
16. A method of treating a chemokine mediated disease state in a mammal suffering from, or at risk of, said disease, which comprises administering to a mammal in  
15 need of such treatment a therapeutically effective amount of a compound as claimed in claims 1 to 12.
17. A process for preparing Anhydrous Form B comprising:
- 20 a. drying a water-wet or hydrated form of a sample of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methylbenzenesulfonamide in the presence of phosphorus pentoxide under reduced pressure; or,
- b. heating a sample of Hydrate Form A from ambient temperature to 100°C.
- 25 18. A process for preparing Anhydrous Form C comprising heating a sample of Hydrate Form B from ambient temperature to 100°C.
19. A process for preparing Hydrate Form A comprising reacting 4-(3,4-dichlorophenoxy)-1,4'-bipiperidine with 4-methylbenzenesulfonyl isocyanate in a  
30 suitable solvent at ambient temperature to form *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in the suitable solvent; adding to that concentrated aqueous sodium hydroxide solution followed by water; and:

- 5           a. stirring the resulting mixture to allow the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide, possibly contaminated with suitable solvent, to precipitate out with Hydrate Form A remaining after filtration and drying, or,
- b. distilling the suitable solvent and allowing Hydrate Form A to precipitate from the aqueous.
- 10   20. A process for preparing Hydrate Form A comprising adding concentrated aqueous sodium hydroxide solution to a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in water at a temperature in the range 30-60°C and allowing the mixture to cool with the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitating and Hydrate Form A remaining after filtering and drying.
- 15   21. A process for preparing Hydrate Form A as claimed in claim 20 comprising:
- a. mixing *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide with water and heating the mixture to a temperature in the range 30-60°C; and,
- 20           b. adding concentrated aqueous sodium hydroxide solution and allowing the mixture to cool with the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitating and Hydrate Form A remaining after filtering and drying.
- 25   22. A process for preparing Hydrate Form A comprising adding concentrated aqueous sodium hydroxide solution to *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a suitable organic solvent; heating the mixture and separating the aqueous layer; adding IMS and, optionally, toluene to the aqueous phase and cooling the resulting mixture; and, filtering off and drying the solid that forms.
- 30

23. A process for preparing Hydrate Form A comprising heating a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form B) and aqueous sodium hydroxide; cooling the mixture and extracting the cooled mixture with dichloromethane; combining the extracts;  
5 optionally reducing the volume of the combined organic extracts; cooling the dichloromethane mixture so that the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitates; and, filtering off and drying the solid that forms.
- 10 24. A process for preparing Hydrate Form A comprising drying a sample of Hydrate Form D under reduced pressure at a temperature in the range 10-100°C.
25. A process for preparing Hydrate Form A comprising drying a sample of Solvated Form E at atmospheric pressure at a temperature in the range 0-30°C.
- 15 26. A process for preparing Hydrate Form B comprising mixing a solution of 4-(3,4-dichlorophenoxy)-1,4'-bipiperidine in tetrahydrofuran with a solution of 4-methylbenzenesulfonyl isocyanate in tetrahydrofuran at a temperature in the range 15-35°C; adding aqueous sodium hydroxide solution and collecting the solid that  
20 precipitates.
27. A process for preparing Hydrate Form C comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water and acetone from reflux to  
25 around 0°C and collecting the solid product that forms.
28. A process for preparing Hydrate Form C comprising drying a sample of Solvated Form E reduced pressure at a temperature in the range 10-100°C.
- 30 29. A process for preparing Hydrate Form D comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water and 2-propanol from 50-80°C to 0-10°C and filtering off the residue.

30. A process for preparing Solvated Form E comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water, IMS and toluene from 50-80°C to 0-10°C and filtering off the residue.
31. A process for preparing *N*-[[4-(3,4-Dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) comprising:
- purifying *N*-[[4-(3,4-dichlorophenoxy)-[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide using reverse phase chromatography eluting with a mixture of aqueous ammonia and acetonitrile; and,
  - freeze drying the fractions containing *N*-[[4-(3,4-dichlorophenoxy)-[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide and triturating the residue with acetonitrile and then drying the residue under reduced pressure at ambient temperature.
32. A process for preparing *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) comprising:
- heating a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide Form B and acetonitrile to 40-60°C; and,
  - drying the solid from the slurry so formed under reduced pressure.